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허혈-재관류 신손상에서의 paricalcitol의 보호 효과

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Paricalcitol Attenuates Ischemia-reperfusion Injury in Mice Kidney

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Background: Ischemia-reperfusion injury (IRI) is unavoidable event in renal transplantation, causing the delayed graft function and increased immunogenicity. We investigated the effects of paricalcitol on mouse model of renal IRI and its potential mechanism related with renoprotective effects.

Methods: Paricalcitol (0.3 μ/Kg) was administered to male C57BL/6 mice 24 hours before IRI, and mice were killed at 72 hours after IRI. The effects of paricalcitol pretreatment were evaluated in terms of modulation of renal inflammation and prostaglandin E2 (PGE2) synthesis.

Results: Treatment with paricalcitol decreased blood urea nitrogen levels, serum creatinine levels, tubular necrosis score. Paricalcitol decreased the number of TUNEL-positive cells and reduced the expression of apoptotic markers. The production of RANTES and tumor necrosis factor-α were reduced by paricalcitol and the infiltration of CD40-positive antigen-presenting cells were decreased in the paricalcitol-treated kidneys. Paricalcitol inhibited the production of Th1 cytokines interleukin (IL)-2 and interferon-γ, which was accompanied with decreased infiltration of T-cells and macrophages. The immunomodulatory effects of paricalcitol also affected the decreased production of Th2 cytokines IL-4 and IL-10. Paricalcitol induced the increased cyclooxygenase (COX)-2 expression and decreased the 15-hydroxyprostaglandin dehydrogenase (15-PGDH) production, which lead to increased endogenous PGE2 synthesis. Of the PGE2 receptors, the expression of EP1 and EP4 were increased in the paricalcitol-treated kidneys and the activation of EP4 receptors increased the expression of survival kinase Akt.

Conclusion: Our study demonstrated that paricalcitol has a protective effect on renal IRI and that this effect is associated with inhibition of renal inflammatory infiltration, increased PGE2 synthesis and EP4 receptor activation.

Key Words: Paricalcitol, 허혈-재관류 손상, 염증
Paricalcitol, Ischemia-reperfusion injury, Inflammation